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Analysis of Control Measures Used During Cholera Outbreaks Among Internally Displaced Persons

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Abstract

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by

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MS, Walden University, 2014

BS, Lynchburg College, 2008

Dissertation Submitted in Partial Fulfillment

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Abstract

Cholera remains a major public health problem affecting high-risk populations such as camps of internally displaced persons. During a cholera outbreak, it is essential to reduce transmission and minimize new infections. The Miasma theory, host-agent-environment model and Ecosocial theory were utilized for this study. This study was a retrospective comparison to determine whether historical cholera control measures are effective during current cholera outbreaks within camps of internally displaced persons. A quantitative approach ascertained changes in incidence and mortality rates following implementation of primary and/or secondary control measures. Cholera outbreaks were identified from the World Health Organization's (WHO) Disease Outbreak News reports issued between 1996 and 2017. Each reported cholera outbreak was categorized into one of eight outbreak cohorts – each cohort having the same primary control measure. The WHO Data Repository was used to identify cholera incidence and/or mortalities and the World Bank data set was used for population total to calculate incidence and/or mortality rates for the years prior to and the year of the outbreak to calculate the case percentage change and death percentage change. Analysis of covariance was used to assess statistical significance in rate change within each intervention cohort. No statistical significance was noted within various cholera control intervention. Limitations of this study provide the basis for continued research on this topic; also aligning with the Global Task Force on Cholera to reduce infections by 90% by the year 2030.

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Chapter 1: Introduction to the Study

Introduction

Throughout the years, cholera outbreaks have plagued many different countries. Cholera is not merely a historical problem; it remains a major public health problem in current society. One population that is especially susceptible to a cholera outbreak consists of internally displaced persons living within camps. During a cholera outbreak, it is essential to the health of a population, especially within camps of internally displaced persons, to reduce transmission and minimize infections. The purpose of this study was to conduct a retrospective comparison to determine if historical cholera control measures are still effective during current cholera outbreaks.

Background

It is estimated that, globally, there are between 3 and 5 million cases of cholera annually. There are approximately 100,000 to 120,000 cholera-related deaths each year. However, these reports do not adequately reflect the global cholera burden due to only approximately 5%-10% of cholera cases actually being reported within underdeveloped settings, where cholera rates are highest (Ali et al, 2012).

Cholera transmission occurs through the fecal-oral route, with epidemics often occurring after natural disasters, civil unrest, violence, and wars (Zuckerman, Rombo, & Fisch, 2007). There are several risk factors for cholera outbreaks; however, a combination of poverty and displacement yields one of the most vulnerable populations (Sim, 2013). Populations of internally displaced persons are not only among the most at-risk groups for cholera outbreaks, but also are more susceptible to the negative health impacts of cholera due to scarcity of resources (such as clean water and sanitation; Sim, 2013). Within 2014, approximately 11 million people were displaced within their own countries, primarily due to violence, which equated to approximately 30,000 people per day (United Nations High Commissioner for Refugees [UNHCR], 2016). As the population of internally displaced persons increases in size, cholera outbreaks will continue to increase, which could lead to increased epidemics and pandemics (Sim, 2013).

Problem Statement

During a cholera outbreak, it is essential to the health of a population to reduce transmission and minimize infections. The World Health Organization (WHO, 2016b) indicates that proper cholera control includes access to clean water, proper waste management, effective sanitation, vector control, increased food safety practices, increased hygiene practices, and increased education and public information. In a systematic literature review, Taylor, Kahawita, Cairncross, and Ensink (2015) highlighted that there are few interventions (such as vaccination campaigns, educational campaigns, and the provision of safe water and sanitation supplies) that have been tested during a cholera outbreak; therefore, there is a knowledge gap regarding which interventions are the most appropriate to use during an outbreak. The effectiveness of recommended cholera control measures has been examined by several researchers, including Ivers et al. (2015) and Lopez, Gonzales, Aldaba, and Nair (2014). However, cholera infections and cholera outbreaks continue to evolve, and intervention strategies need to adapt. In addition, *V. cholera* has evolved with two significant modifications over the years, including both a new lipopolysaccharide structure and a new serotype (Ryan, 2011). It is essential to understand how these changes impact current control measures and whether these measures remain effective. In this study, I sought to examine if historical control measures are still effective during current cholera outbreaks.

Purpose of the Study

The purpose of this study was to conduct a retrospective comparison to determine whether historical control measures are still effective during current cholera outbreaks. A retrospective comparison allowed for the examination of pre-existing longitudinal data from cholera outbreaks. Per the Belmont Report, it would not be ethical to conduct a prospective study to examine cholera control measures, in that it would not be ethical to withhold applications of accepted best prevention practices from those in need (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979).

Historical research has shown the effectiveness of control measures; however, analysis of these control measures in the present day is lacking (Ivers et al., 2015; Lopez et al., 2014). To address this gap, a quantitative approach was used. Data from outbreaks within camps of internally displaced persons were used to ensure that similar characteristics and parameters within the outbreaks (such as sanitation conditions and clean water supplies) were maintained. WHO incidence and fatality data from outbreaks occurring between 1995 and 2017 were examined prior to and after implementation of a control measure to determine how that control measure impacted incidence and mortality rates. Incidence and mortality rate data were obtained on those outbreaks that were reported to the WHO. Within underdeveloped settings, WHO-reported rates are lower than actual incidence and mortality rates. Surveillance within camps of internally displaced persons are also limited due to inadequate communication and coordination strategies (Centers for Disease Control and Prevention [CDC], 2010). This is a known limitation of cholera surveillance (both in underdeveloped settings and within camps of internally displaced persons) and was examined during analysis. Due to estimations that only 5%-10% of cholera cases are reported (within underdeveloped settings), results from this analysis can be used to estimate more realistic rates (Ali et al., 2012). Because this retrospective comparison focused on camps of internally displaced persons, reported incidence and mortality rates should be more reliable and more accurate than those within undeveloped settings, due to increased surveillance efforts within these camps. Theoretically, cholera prevention and control measures should have more influence within these camps; however, outbreaks are still occurring regularly, with severe health consequences.

Research Question

The study's quantitative research question was the following: Did the cholera incidence rate and/or mortality rate change after the implementation of specific control measures/combinations of control measures (proper sanitation, vaccination, and education) within groups of internally displaced persons that experienced a cholera outbreak between the years of 1996 and 2017?

Conceptual Framework

Two theoretical frameworks were used for this study: the host-agent-environment model and the ecosocial theory of disease. Edwin Chadwick, a supporter of the miasma theory, contended that the living conditions of the poor contributed to disease transmission (Chadwick, 1984, 1842; Science Museum, n.d.). His work, which showed a direct link between the living conditions of the poor and disease as well as life expectancy, led to the Public Health Act of 1848 (Chadwick, 1984, 1842; Science Museum, n.d.).

Known as the traditional model of epidemiology, the host-agent-environment model describes interactions between individuals and their environment (Kellam, Koretz, & Moscicki, 1999). This epidemiological model displaced the miasma theory (which suggested that diseases were a result of dirty air) due to John Snow's work determining that the source of cholera is infection with *V. cholera* through fecal-oral transmission (Kukaswadia, 2013; Snow, 1855). The epidemiological model is essential to research on disease transmission and examinations of the distribution and determinants of disease occurrence, which are essential for developing and evaluating the effectiveness of disease control measures.

Ecosocial theory may be used to explain disease distributions within populations. This theory encompasses embodiment; pathways of embodiment; the interplay between exposure, susceptibility, and resistance; and accountability. This theory was important to this research because it allows researchers to explain disease patterns due to biological and social influences (Krieger, 1994).

Nature of the Study

The nature of this study was quantitative. This study entailed retrospective comparison of different control measures as different cohorts. A quantitative approach allowed for this comparison and statistical analysis of the data. Adjusted statistics were used to enable fair comparisons among the cohorts. To ensure that the comparisons were objective, studied outbreaks included those occurring within camps of internally displaced individuals. Comparability was greater within UN camps that included UN staff. Any other confounding variables (such as geographical location, population dynamics, camp management, and time period of outbreak) were adjusted through statistical analysis (through statistical methods such as stratification or analysis of covariance [ANCOVA]) to make them comparable.

Definitions

Per the WHO (2016b), a clinical case definition of cholera is a positive laboratory test of the presence of *V. cholerae* within a stool sample. For this analysis, a cholera case was defined as a positive test result for the presence of *V. cholerae.* Per this definition, a cholera case might or might not be accompanied by any signs or symptoms of infection; however, testing for *V. cholerae* is generally conducted after the presence of signs/symptoms are observed. Per the *Dictionary of Epidemiology*, a disease outbreak is defined as a localized increase in disease incidence (Porta, 2014). This definition was used to classify cholera outbreaks and is not dependent upon the presence of infection symptoms. Internally displaced persons are refugees who remain within their own country (UNHCR, 2016). Camps of internally displaced persons are congregations of these refugees. This definition was used for camps of internally displaced persons.

Assumptions

There were several assumptions in this analysis. One assumption was that the camps of internally displaced persons were similar in nature and characteristics, meaning that the availability (or lack of) resources was consistent across the camps. Another assumption was that all persons within those camps had the same probability of and susceptibility to cholera infection due to the population densities of the camps. Well-planned facilities can be taxed with overcrowding and depleted resources, which can exacerbate cholera transmission.

Scope and Delimitations

The data examined were for the years 1996 to 2017 only, due to the availability of Disease Outbreak News reports (DONs) with detailed information on cholera outbreaks and responses (WHO, 2016a). In addition, cholera outbreaks that were included in this analysis were limited to those occurring within camps of internally displaced persons. This allowed for consistency across the outbreaks for analysis.

Limitations

There were several limitations to this analysis. This analysis focused only on reported cholera cases. The definition of a cholera outbreak that was used did not necessitate the presence of infection symptoms. It is not routine to test for *V. cholera* infection in the absence of symptoms. Surveillance of cholera is a limitation to any analysis involving cholera due to the underreporting of cases. This limitation was minimized by focusing on camps of internally displaced persons, where surveillance efforts should have been more robust. In addition, this analysis focused on confirmed cases of cholera, potentially excluding more cases of cholera from the analysis.

Significance

As of 2016, there were approximately 65.3 million internally displaced persons or refuges globally. This was the highest level of displacement to date (UNHCR, 2016). With increasing numbers of displaced individuals, the risk of a cholera outbreak also increases. As these numbers continue to climb, it is essential to reduce disease transmission effectively among camps of internally displaced persons. These individuals face several hardships; they should not be burdened with additional health issues, including cholera infections.

This research was conducted to fill a knowledge gap about whether historical control measures that are still employed during outbreaks are effective during current/present-day cholera outbreaks within camps of internally displaced persons. This knowledge is essential to public health officials who are responding to an outbreak in order to reduce the negative health impact that cholera has on vulnerable populations.

This research was unique in that I examined historical control measures within present-day outbreaks to determine the effectiveness of these methods in present times. Previous research has focused on the effectiveness of control measures; however, an examination of these control measures in the present day is lacking.

This research has the potential to highlight the effectiveness of current control measures. If historical control measures are found to be ineffective, this research may provide a basis for further research and policy development. It has the potential to lead to the development of new control measures that are more effective in outbreak management. This research could potentially change the way in which officials respond to cholera outbreaks so that disease-related health consequences are mitigated. If historical control measures are found to be effective, further research can be conducted to examine current policy and intervention management. As cholera outbreaks continue to occur, it may be that the control measures are appropriate; however, the implementation requires further research. In addition, results from this study may be used to further research on control measures for similar diarrheal diseases that occur during wars and times of crisis, such as dysentery and typhoid fever infections (Sharma, 2001).

The knowledge gained from this research may provide public health officials a basis for further research into cholera control measures and policies that are applicable to outbreaks occurring among camps of internally displaced persons. In addition, the knowledge gained from this research could not only improve the health of those individuals who are displaced by reducing cholera's impact, but also could save lives from preventable/treatable disease. Individuals are fleeing to these camps for various reasons, and reducing negative health consequences for these displaced populations could not only increase quality of life, but also save lives.

Summary

In summary, this study involved a retrospective comparison. Data from 1996 to 2017 were used for analysis to determine whether historical control measures are still effective during current cholera outbreaks. If historical control measures are found to be ineffective, this research may provide a basis for further research and policy development; if they are found to be effective, further research may be conducted to examine current policy and intervention management. This study may support positive social change by informing more effective cholera control management among camps of internally displaced persons.

Chapter 2: Literature Review

Introduction

Cholera is a not a new disease; however, it still affects a large number of communities each year. Despite the existence of several cholera control measures, the mortality rate for the disease remains high, at 6.3 deaths per 100,000 people (Ali et al., 2012). High rates of malnutrition, morbidity, and mortality are seen in populations that have been forced to migrate, such as populations within internally displaced camps (CDC, 1992). Within these camps, morbidity and mortality rates can reach 60 times those of nonrefugee populations, with the main causes of death being diarrheal diseases such as cholera (Connolly et al., 2004). This chapter provides a review of relevant conceptual frameworks and theories, the history of cholera, cholera epidemiology, control measures used during cholera outbreaks, and how cholera affects camps of internally displaced persons.

Search Strategy

The research described in this chapter was compiled from an extensive review of available literature. A review of CDC and WHO websites provided a foundation of cholera-related material and cholera control strategies. A search was conducted within PubMed using the terms *cholera control measures* for works published since 2015. The following terms were also searched within PubMed: *Asiatic cholera, history of Asiatic cholera, the host-agent-environment model, germ theory, and John Graunt*. In addition, Google Scholar was used to identify many appropriate sources. The search terms used included *cholera, cholera transmission, cholera control measures, history of cholera,*

cholera prevention, cholera vaccines, what is lacking in cholera control, cholera prevention strategies, *cholera epidemiology, cholera pandemics, cholera epidemics, cholera water quality interventions, internally displaced persons, camps of internally displaced persons, cholera in camps of internally displaced persons, John Snow, miasma theory, ecosocial theory, history of vaccines, host-agent-environment model, Bradford Hill criteria,* and *web of causation.*

Conceptual Framework

Several conceptual frameworks and theories are relevant to the history of cholera transmission. The early miasma theory once defined dominant beliefs about disease transmission. This theory evolved into a more complex theory with greater explanatory power in relation to disease. The host-agent-environment model, known as the traditional model of epidemiology advocated by John Snow, explains disease transmission, and the ecosocial theory provides a construct for disease distribution.

Miasma Theory

Among primitive tribes and ancient cultures, primitive ideas regarding sickness transmission centered around contact with others. Epidemics were rare in small communities; however, they began to have devastating effects once population density increased. This led people to magical or religious disease explanations. Diseases were thought to be punishment of one’s sins from the gods or caused by evil spirits or demons that needed to be exorcized (Karamanou, Panayiotakopoulos, Tsoucalas, Kousoulis, & Androutsos, 2012).

Hippocrates, born in 460 BC and known as the father of Western medicine, was among the first to regard disease as a natural occurrence rather than a supernatural phenomenon. His beliefs focused not on magical miasmata but on contagion (Pappas, Kiriaze, & Falagas, 2008). In the sixth century, philosophers began to associate the environment with health and diseases. Geography and meteorology began to be correlated with diseases. This led to the development of theories on how the atmosphere was associated with diseases, which developed further into miasma theory. According to miasma theory, the air is contaminated with poisonous vapors or "miasmas" that are produced by organic matter. These "miasmas" can invade the body, disturbing vital functions and resulting in a person becoming sick. Major natural disturbances, such as earthquakes and comets, were said to charge the air with miasmas (Karamanou et al., 2012).

In the 17th century, John Graunt refuted evidence of disease transmission by contagion (Graunt, 1662; Rothman, 1996). At the time, disease occurrence was thought to be provoked by the alignment of the planets, and disease transmission occurred via miasmas that emanated from bodies of those who were sick. Graunt's analysis of mortality rates showed that outbreaks, specifically the Black Death, were not synchronized with political or astrological events (Graunt, 1662; Morabia, 2013). His belief in the miasma theory was strengthened with his work with the *Bills of Mortality*, in which he determined that individuals who lived in crowded areas were more likely to get sick than those who lived in noncrowded areas due to larger amounts of pollution within the air, lack of proper sanitation practices (such as sewer systems), and large amounts of sick people (Graunt, 1662).

The miasma theory, dating back to the fifth century BC, was the dominant theory of why people were sick. This theory attributed sickness to foul emanations. Within England, industrialization and urbanization during the 19th century led to the enclosure of open land, thus altering the morbidity and mortality profile drastically. This affected both the perception and the nature of the health problems that the country faced. Sanitation discoveries followed, prompting more studies of food and water pollution and occupational hazards. These studies brought significant reinforcement of the miasma theory (Susser, 1998). In 1842, Chadwick, a firm believer in the miasma theory, published his *Report on the Sanitary Condition of the Labouring Population of Great Britain*, in which he argued for drainage improvements in order to remove foul smells from homes and to reduce disease. The miasma theory was widely believed into the 1800s and was one of the main explanations of cholera and cholera transmission (Karamanou et al., 2012).

The Host-Agent-Environment Model (the Epidemiological Triangle)

The origin of the host-agent-environment model can be traced to historical phenomena that seemed inexplicable at the time, such as why not all people who are infected develop a disease and why not all people who are exposed to a disease become infected. Explanations of such phenomena evolved from an agent-driven framework to a host-agent-environment framework. The new framework identified an *agent* (an exogenous entity) that acts upon a *host*. The agent is typically an infectious pathogen or microorganism, such as a parasite, bacterium, virus, or other microbe. The agent must be present for infection; however, presence of the agent does not always cause the disease. Over the years, the meaning of the term *agent* has broadened to include both physical and chemical causes of disease. The term *host* refers to the individual who gets the disease. There are several factors that influence an individual's exposure, response, or susceptibility to the agent. The term *environment* encompasses both the natural world and social institutions and practices (Leavell & Clark, 1958; Porta, 2014;). This model is important to research on cholera because cholera infection stems from an infection with *V. cholera* (agent) that acts on a host (individual or population) within a specific environment (either a community or country).

In the 19th century, proponents of germ theory suggested that some diseases were caused by infectious agents. Germ theory's explanation of disease causality focused on infection with microorganisms (Koch, 1881). Koch (1881) developed a reproducible and scientific method for isolating microbial cultures that led to the identification and characterization of many causal organisms of diseases, including tuberculosis, cholera, and anthrax. This led to advancement in the understanding of many diseases, which subsequently led to the development of immunizations for many of these diseases. This research was fundamental in supporting germ theory and contributing to the understanding that many diseases are contagious (Koch, 1881).

The Bradford Hill criteria for causality, proposed in 1965, are a flexible set of guidelines that are used to evaluate relationships between exposures and disease outcomes and to aid in causal inference. The Bradford Hill criteria are nine items used to determine whether epidemiological associations are causal. Criterion 1 is strength of association, with a strong association indicating greater likelihood of causality (related to the current concept of statistical significance). Criterion 2 is consistency, meaning that a consistent association is replicable across different researchers, different studies and different populations. Criterion 3 is specificity, meaning that an association is more likely to be causal when exposure only causes that one disease. Criterion 4, temporality, is universally accepted among researchers; this criterion indicates that exposure must precede the disease in order for the association to be causal. Criterion 5, biological gradient, applies to the notion that there is a dose-response between exposure and effect. Criterion 6, plausibility, means that epidemiology and biology interact. For a cholera case, plausibility refers to *V. cholera* biologically interacting with the body to produce an epidemiological response. Criterion 7, coherence (similar in nature to Criterion 6), refers to the association making sense per the knowledge that is available. Criterion 8, experiment, means that evidence from experimental manipulations supports the causal inference. The last criterion, analogy, suggests that once a causal relationship is identified, researchers should accept weaker evidence of a similar agent's causal inference to a similar disease (Fedak, Bernal, Capshaw, & Gross, 2015).

Ecosocial Theory

Ecosocial theory describes disease distribution by examining how individuals' social interactions impact their biological response. The name of this theory incorporates the prefix *eco*, stemming from the word *ecology*, which is the study of evolving interactions between organisms and inanimate matter over time and space (Leavell & Clark, 1958).

There are five core aspects of ecosocial theory: scale, level of organization, dynamic state, mathematical modeling, and understanding the phenomena with regard to general processes. *Scale* refers to quantifiable dimensions that are observed, such as number of cholera cases or outbreaks. *Level of organization* refers to the specified nested hierarchies, such as communities or households, that are infected with cholera. *Dynamic state* refers to the interplay of inanimate and animate inputs/outputs with knowledge that the phenomena and process may be scale dependent. *Mathematical modeling* refers to how groupings of organisms work together using both detailed synthetic and idealized minimal models. *Understanding the phenomena with regard to general processes* refers to how two of the same things (such as organisms or populations) share common important processes and features but are not identical (Leavell & Clark, 1958).

Ecosocial theory provides a theoretical checklist for epidemiological research. It focuses on questions of what or who determines current and/or changing patterns of social health inequalities. In relation to cholera, this theory may be applied to examine what causes cholera outbreaks within certain populations. The ecosocial approach combines biological and ecological analysis with the social production of disease perspective. Ecosocial constructs include embodiment; pathways of embodiment; interplay of exposure, resistance, and susceptibility; and finally accountability and agency. *Embodiment* refers to how people biologically incorporate the world in which they live. No aspect of someone's biology can be understood without knowing the person's history and societal ways of living. With regard to cholera, how does cholera impact someone biologically, and where is the exposure coming from? *Pathways of embodiment* are the possibilities and constraints of an individual's biology. It also involves societal arrangements of property and power that are contingent on consumption, production, and reproduction. With regard to cholera, how do individuals' societal arrangements (such as economic status) impact their susceptibility and probability of cholera infection? *Interplay of exposure, resistance, and susceptibility* refers to the relationship of each factor and its distribution within the pathways of embodiment. *Accountability and agency* involve institutions, households, individuals, scientists, and epidemiologists being accountable and considering both the benefits and limitations of their analysis. This construct renders both institutions (such as government agencies) and researchers accountable for their actions in regard to not only their research, but also their efforts to supply necessary aid. With these constructs, social relations and biological expressions can be used to examine and explain population patterns of disease, thus contributing to the ability to generate new knowledge (Leavell & Clark, 1958). The use of ecosocial theory allows researchers to examine how cholera is transmitted in different populations and societies.

History of Cholera

Early importations of cholera can be traced from India into neighboring and close countries. The earliest evidence of cholera can be found in ancient India, where it referred to as *Asiatic cholera*. Macnamara (1876) reported that although cholera was observed, it had not been observed as an epidemic. It was reported that people within the

Lower Bengal worshipped the goddess of cholera in attempts to ward off the terrible disease. Although these reports show cholera in ancient India, the more irrefutable evidence of cholera is found within records of European observers who were exposed to cholera after the arrival of Vasco da Gama in 1498 AD on the coast of Malabar. Gaspar Correa documented two outbreaks of cholera: (a) one in 1503 among the army of the sovereign of Calicut, in which men did not last more than 8 hours after symptoms occurred, and (b) another outbreak in 1543, in which the fatality rate was so high that it was difficult to bury all of those who had died. Between 1503 and 1817, cholera cases continued to be reported by the Portuguese, followed by the Dutch and the French, and then finally the British (Macnamara, 1876; Pollitzer, 1954). It is important to note that the establishment of the Hospital Board within Madras and Calcutta did not occur until 1786; therefore, regular reports of cholera among the Europeans and native soldiers are unavailable. However, sufficient evidence exists proving that both the east and west coasts of India had incidents of cholera infections (Macnamara, 1892). Although prevalent, cholera had not manifested as a true epidemic. Before the 19th century, there were no observations of a long-distance spread of cholera westward from India, with the exception of reports of cholera in eastern China. It has been reported that within China, cholera cases date back to the 7th century (Macnamara, 1876; Pollitzer, 1954).

Cholera Pandemics

In 1817, a new period in cholera history began, with the first onset of a series of pandemics. This was the first instance of wide, long-distance spread from the Middle East to Europe for cholera, which many claimed was a more localized disease (Glass &

Black, 1992). Within India, the years 1815 and 1817 brought heavy rainfalls, floods, and harvest destruction, producing increased cholera devastation. It was in 1820 that cholera was transmitted via the sea-route transmission to Bangkok. In 1821, infections started to become more localized again. Japan did not encounter cholera until 1822, when a merchant ship brought the infection, which rapidly took lives. In the same year, the Persian Gulf was struck, and within 3 weeks, over 18,000 people had died. The disease continued to spread northward and eventually reached European territory. The severe winter of 1823-1824 was a contributing factor in cholera not progressing further that year. In addition to this continuous spread, cholera spread long distance to Mauritius in 1819 and the coast of Africa in 1820-1821 (Macnamara, 1876; Pollitzer, 1954).

The second pandemic of cholera can be traced back to India, where increased numbers of violent infections were seen in 1826. This pandemic impacted the Jumna and Ganges Rivers in 1827, Afghanistan and European Russia in 1829, and then Persia, Europe and Africa in early 1830. Every possible effort was made to stop the spread of cholera; however, it steadily advanced into Russia, reaching Moscow in 1830. In the spring of 1831, infections reached the war-stricken country of Poland, where both Russian and Polish troops were impacted. Infections within these troops contributed to the westward spread of the infection. In 1831, the disease spread across England, resulting in 14,796 reported cases and 5,432 deaths. At the end of 1832, cholera appeared in Ireland, Germany, France, Belgium, and the Netherlands. Also in 1832, cholera hit the shores of North America, as well as Peru and Chile. In 1833, cholera spread to Cuba and Spain, and by 1834, cholera had reached Norway, producing a severe epidemic (Chan, Tuite, & Fisman, 2013; Pollitzer, 1954; Wu, Chen, Pollitzer, & Wu, 1934;).

The third pandemic is more difficult to trace than the previous two due to several disease importations. In 1852, cholera was raging in India and within 1853 it was rampant in northern Europe, Mexico, the USA, and the West Indies. In 1854, cholera could be found in Greece, Turkey, Canada, and Colombia. The year 1854 is deemed one of the worse years in cholera history on record (Macnamara, 1876; Pollitzer, 1954). It was at this time that it was determined that cholera stemmed from a contaminated water supply; therefore, safe drinking water was critical to reducing disease transmission (Snow, 1856). There were many reappearances of cholera in 1855, including, Asia Minor, Syria, Africa, Egypt, Sudan, Morocco, Italy, Austria, Switzerland, Venezuela, and Brazil. Between 1856 and 1858, cholera raged havoc in Spain, Portugal, Philippines, Korea, and India. In 1859, Europe appeared to be free of cholera (Macnamara, 1876; Pollitzer, 1954).

The fourth pandemic lasted from 1863 to 1879. New traffic routes, that were newly developed, were attributed to the spread of cholera during this timeframe, with cholera spreading into Egypt, Italy, southern France, and Constantinople. Although debates on how cholera reached Mecca still occur, it is certain that conditions were extremely favorable for transmission among the large numbers of pilgrims that were assembled. It is estimated that over one third of the pilgrims fell victim to cholera. These pilgrims spread cholera to Mesopotamia, Palestine, Arabia, Suez, and Syria. This lead to Alexandria becoming a distribution center of the disease in which refugees carried the disease into Egypt, Istanbul, and the Mediterranean. Russia was infected by various transmission routes; however, the country suffered little with the infections being restricted to only six governments. Italy, Spain, France, Sweden, and Germany were severely impacted during this pandemic (Colwell, 1996; Pollitzer, 1954).

The U.S. was plagued with a cholera epidemic in 1832, within New York City. This resulted in over 3,500 deaths of a population of approximately 250,000. This epidemic exposed major class, religion, and race divisions within the city as those impacted the hardest were from the poorer neighborhoods, mainly inhabited by African Americans and Irish Catholics. In 1849, another epidemic in New York City produced over 5,000 deaths in a population of approximately 500,000 due to the population doubling (Wilford, 2008).

The fifth pandemic lasted from 1881 to 1896. This pandemic caused less damage than its predecessors. At this time, it was determined that cholera was the result of a gastro-intestinal infection and the beginning of cholera control measures emerged. Once again, cholera spread through Italy, France, and Spain. Quarantine measures were put in place in an attempt to protect Italy; however, it caused havoc within Naples with more than 10,000 cases and more than 5,000 deaths (Colwell, 1996; Pollitzer, 1954).

The Sanitary Movement of the 19th century led to an increase on the importance of hygiene and sanitation (Pizzi, 2002). The Seamen's Hospital Society built a hospital at Albert dock in 1890. In 1899, the hospital was partnered with the London School of Tropical Medicine, which was concerned with medical education. In 1905, the School of Tropical Medicine was expanded with the joining of the Lister Institute of Preventive

Medicine, which focused on hygiene and pathology (Acheson & Poole, 1991). In 1916, the School of Hygiene and Public Health at Johns Hopkins was founded. This school was also funded by the Rockefeller Foundation, which aimed to strengthen its role in not only improving medical education but also in conducting global, targeted campaigns against diseases, including malaria, yellow fever, and hookworm. This particular school evolved to be the model for public health education, with superior faculty working in sanitation, medicine and bacteriology (The Rockefeller Foundation, n.d.).

Beginning in 1859, London's government contracted the development of an underground sewer system that included 1,100 miles of street sewers and 82 miles of intercepting sewers (BBC, 2014). Importation of cholera into the United States, by an infected ship, was averted through the correct diagnosis via laboratory methods. In 1892, an infected water supply led to an explosive outbreak in Hamburg, Germany. Over 250 other communities in Germany were also impacted; however, the cases were sporadic. In the same year, eight severely infected ships arrived in New York. The infection was contained through appropriate control measures that were facilitated by the city health laboratory (Colwell, 1996; Pollitzer, 1954).

The fifth pandemic did not completely resolve, and in the beginning of 1899, the sixth pandemic begun. This pandemic lasted until 1923 and had a causal connection to the exacerbated cholera situation within India. Once again, the disease spread westwards, in 1900, and eastwards in 1902. Even though all available precautions were implemented, cholera still invaded Egypt and claimed approximately 34,000 victims within three months. During World War I, specifically in 1915, cholera became widespread yet again. Wars and civil unrest lead to population displacement, disruption of basic public health services and food shortages, which provided a high-risk environment for cholera and cholera transmission (Toole & Waldman, 1997). The years of 1918, 1920 and 1921 were noted with high incidence rates. A decline in incidences began in 1923, with only sporadic cases noted in 1924 and 1925. Many believed that cholera pandemics would not reoccur due to global improvements in sanitation and water supplies (Barua, 1972; Pollitzer, 1954). In 1961, the seventh (and current) pandemic began in Indonesia. It spread through Asia to Europe, Latin American and Africa. It is believed that this pandemic is a result of the new serotype of *V. cholera* (Harris, LaRocque, Qadri, Ryan, & Calderwood, 2012).

Edwin Chadwick

In the 1800s, Edwin Chadwick was known as one of the most important public health activists. One of Chadwick's driving forces was to use science for social improvement. In 1832, Chadwick served on the royal commission in which he was tasked with investigating how effective the Poor Laws were. His investigations prompted his interest in sanitation problems. Chadwick was a firm believer of the miasma theories and believed that if people were healthier, from measures such as cleaning and proper ventilation, they would be less dependent on welfare. After cholera appearances in 1831, 1837, and 1838, the government asked Chadwick to investigate sanitation. In 1842, Chadwick published *The Sanitary Conditions of the Labouring Population,* in which he showed a direct link between the living conditions of the poor and diseases (Chadwick, 1842; Science Museum, n.d.). Chadwick's research further strengthened the observations of John Graunt, who observed that individuals that lived in crowded areas were more likely to get sick over those who lived in non-crowded areas (Graunt, 1662). Chadwick's publication was one of the driving forces for the Public Health Act of 1848 (Chadwick, 1842; Science Museum, n.d.).

John Snow

John Snow is most recognized for his contributions during the 1853 and 1854 cholera epidemics in London (Vandenbroucke, Eelkman Rooda, & Beukers, 1991). Snow did not stop the cholera outbreak in London; however, he was very influential to the municipal authority's decision to remove the handle of the Broad Street Pump, which resulted in a significant decrease in cholera infections. Snow suspected that the cause of cholera was an agent that was too small for the naked eye to see but was capable of reproduction and has a similar construction to that of a cell. Unlike other scientists of the time, Snow was more interested in how the disease was transmitted rather than the actual causal agent. He was also a skeptic of the miasmatic cholera theories of the time, due to his extensive work with anesthesia and inhaled gases (Paneth, 2004; Snow, 1849).

Snow's work with cholera illustrates one of the fundamental principles of communicable diseases; the mode of communication. Once the mode of communication is identified, preventative measures can follow. Snow was able to establish the mode of communication of cholera by comparing death rates in a London neighborhood with two different water supplies. One water supply came from the Thames River, upstream from London, and the other water supply came from within the city, just below where the sewer systems poured in. In his research, Snow was only able to count deaths, as information on all cases was not available. It was a difficult task to determine which water supply went to which house as many tenants had fled, others had died, or rent records were incomplete, along with the fact that Snow did not know how many houses each water source supplied. It was not until Snow determined that the water supply from the Thames River was chemically different from the other water supply, that he was able to determine which houses were supplied by which water supply. Snow visited 658 homes, where someone had died from cholera, to determine the water supply to the house. It was not for another two years when he received the detailed breakdown of the water supply system that Snow was able to confirm the correctness of his previous conclusions (Paneth, 2004; Snow, 1855, 1856).

Reverend Henry Whitehead, a minister at St. Luke's Church in Soho, held a different viewpoint than Snow's theory of contaminated water. With the cholera outbreak of 1854, Whitehead became concerned for his parishioners, who were turning to the church for answers, and began to search for answers. Whitehead believed that the outbreak was not due to contaminated water, but rather due to God's vengeance. With that though, he was determined to find a way to alleviate God's anger and thus free his people from this deadly disease. Whitehead had knowledge of Snow's theory and was determined to prove him wrong. Instead of proving him wrong, Whitehead's investigations actually supported Snow's theory. Snow's investigations led him to St. Luke's church; however, he lacked the local knowledge that Whitehead possessed. Even with opposing viewpoints, they began to work together, which eventually led Snow to determine the case of Frances Lewis as the index case for the cholera outbreak (Daniel & Markoff, 2017: Tuthill, 2003).

Due to his work in the mode of communication, Snow was able to specify the mechanisms in which poverty increased cholera transmission. The lack of soap and water (to not only wash one's hands, but also one's clothes), lack of light (to see any soiling), lack of hygienic behavior and education, and unsanitary work practices (often leaving workers to defecate where they ate) all increased cholera transmission opportunities. Snow's opponents believed that poverty invoked other characteristics, such as heavy drinking, which was the cause of higher transmission rates (Paneth, 2004).

Cholera Epidemiology

Cholera is caused by an infection of the bacterium *V. cholera*, which strictly affects a person's intestines. This bacterium produces several different toxins within the host. The most dehydrating symptoms are caused by the cholera enterotoxin, which binds to the intestinal mucosal cells and then activates the adenylate cyclase enzyme. Activation of this enzyme leads to increased intracellular cyclic adenosine monophosphate. This causes the intestinal mucosal cells to excrete large amounts of electrolytes and water, producing severe dehydration in the host (Zuckerman et al., 2007).

Cholera is a diarrheal disease the can affect both indigenous populations and those traveling in/out of an area. Within travelers, it is estimated that 80% of diarrhoeal episodes are caused by a bacterial infection (including cholera). Approximately 90% of all cholera cases are classified as either mild or moderate in severity, with most being difficult to distinguish from other causes. The health status of an individual is a key indicator if the cholera infection will be severe in nature. In healthy individuals, approximately 10^5-10^8 bacteria are needed for infection. Smaller amounts are needed in certain populations, for example, those with low gastric acid levels or low socioeconomic status. Gastric acidity is a major determinant of the severity of the infection due to the natural barrier that natural gastric acid provides. Someone with achlorhydria or hypochlorhydia are at a greater risk of cholera infection from a low level of bacterium. In severe cases, cholera can prove to be fatal and can lead up to a 50% mortality rate if left untreated. The mortality rate can be reduced to 1% if fluid replacement therapy and supportive treatment is administered immediately (Zuckerman et al., 2007).

Cholera is transmitted via the fecal-oral route with individuals becoming infected when they ingest water or food that is contaminated with fecal matter containing *V. cholera* (Edward & Nyerere, 2015). Most epidemics occur after natural disasters, war, or civil unrest due to limited water, contaminated food supplies, limited sanitation and crowded living conditions. Cholera epidemics are characteristically explosive when it is introduced into populations that lack proper immunity and infrastructure (Zuckerman et al., 2007).

According to Ryan (2011) recent outbreaks within Zimbabwe, Pakistan, and Haiti show that cholera action plans are failing and new discussions are needed in response to the global cholera situation. In the past 20 years, *V. cholera* has evolved with two significant modifications over the years that include both a new lipopolysaccharide structure and a new serotype. The new cholera strain may have more severe clinical implications and is quickly replacing the old strain in many areas. It is predicted that this could attribute to the increased cholera fatality rates. With the cholera strain showing this adaptability, it is recommended that cholera control measures are re-examined and possibly adapted (Ryan, 2011).

Lugomela et al. (2014), examined potential relationships between climatic and environmental indices with regards to cholera cases within coastal regions. Between 2004 and 2010, 50% of cholera cases (and 40% of the total mortality) within Tanzania were attributed to coastal regions that only encompassed 21% of the total population. Significant co-variations were found between ocean parameters and seasonally adjusted cholera cases. This model suggested that not only cholera outbreaks but the severity of that outbreak, within this region, can be predicted by oceanic parameters and both climate and environmental parameters may be used to predict future outbreaks (Lugomela et al, 2014).

Surveillance and Reporting

Due to regulations, cholera infections must be reported to the WHO. It is estimated that there are between 3 to 5 million global cases of cholera annually with 100.000 to 120,000 cholera related deaths each year. Cholera prevalence rates show no sign of decreasing and reports from 2005 actually show an increase in cases when compared to previous years. However, these reports do not adequately reflect the global cholera burden due to only approximately 5-10% of cholera cases actually being reported within underdeveloped settings, in which cholera rates are at its highest (Ali et al, 2012).

There are several reasons for cholera cases to remain unreported. When symptoms are mild, health advice may not be sought out by patients. Mild cases may not be tested for *V. cholera,* due to symptoms being indistinguishable from other causes. In addition, there are several surveillance and reporting limitations. Economic disincentives, such as trade sanctions and tourism limitations, can be detrimental for a country's economy, thus promoting a country to underestimate and underreport the true cholera burden. This underreporting has important health consequences for both the indigenous population and any travelers to the area. Health intervention implementation and travel risk assessments rely on accurate disease prevalence rates. Since the 1980s, global travel has seen a significant increase, with 2004 reports indicating that there were over 763 million international tourists (Zuckerman et al., 2007).

Cholera Control Measures

There are several cholera control measures that can be implemented during an outbreak. Per the WHO, the main cholera control strategies include proper case management, training for proper case management, sufficient medical supplies, clean water access, effective sanitation, proper sanitation, enhanced hygiene, enhanced food safety, improved communication, and improved public education (WHO, 2016c). All of these control measures have been used as a single control measure along with being used in conjunction with other interventions; however, current outbreak control activities have been proven insufficient in large-scale outbreaks (Luquero et al., 2013). Mathematical modeling has also been used to understand the efficiency of control measures.

Water Quality and Sanitation Interventions

In the early 1800s, Louis-Bernard Guyton de Morveau and William Cumberland Cruikshank were the first scientists to suggest adding chlorine to water for disinfection to prevent the transmission of water-borne diseases. Chlorination can react with compounds found naturally in the water supply thus producing carcinogenic byproducts. Due to these carcinogenic byproducts, chlorination practices must be regularly monitored. When compared to inadequate disinfection, the WHO states that the risks associated with chlorination are low (Edward & Nyerere, 2015). In a systematic literature review, Taylor et al. (2015) reviewed multiple studies involving well chlorination within cholera outbreaks in Africa. Chlorination was found to be ineffective in controlling cholera and in some cases it actually increased the risk of cholera infection (due to residents discontinuing well use because to safety concerns with the chlorination) (Taylor et al., 2015).

Cholera epidemics can be linked to contaminated drinking water. Lack of safe drinking water increases prevalence of cholera cases. In 2012 in Pondicherry, heavy rainfalls, associated with cyclone Thane, contributed to a cholera outbreak. This outbreak was attributed to contaminated water distribution pipelines from broken and leaking pipes. Within this community, the attack rates were 0.3 to 7%, whereas refugee-camp settings have attack rates over 5%. Community members were urged to boil their water before consumption; however, people were prevented from this measure due to the short supply of cooking-gas. Residents who consumed bottle water were unaffected. The short-term control measures that were initiated included the cessation of water distribution, to repair the damaged pipes followed by chlorination, and flushing of the system. In addition, safe water was provided, along with the establishment of medical camps. Intensive education campaigns were conducted. Long-term measures included extensive reorganization and construction of the water infrastructure (Frederick et al., 2015).

The intervention of improving water quality has been shown to have a lower impact on cholera transmission over other interventions, such as sanitation and hygiene. In many developed countries, water is collected from communal sources that can be large distances from the household. Contamination of water either at the source of or during transport is a major concern. Post-source contamination results in decreased water quality and could negate any improvements made to the water source (Gundry, Wright, & Conroy, 2004).

In a systematic review, Gundry et al. (2004) examined water interventions in regard to cholera. Those interventions that involved water treatment and improved water storage conditions were shown to successfully prevent further cholera transmission. Interventions need to not only consider the water source but also any storage at the household level. Although the review supported the effectiveness of water interventions, there were several limitations noted. Within some of the studies, those who participated in the studies knew of the anticipated outcomes and could have potentially modified their responses. Within other studies, attempts were made to blind the participants. Most water interventions also include some form of educational interventions on proper water handling and hygiene practices (Gundry et al., 2004).

There are conflicting opinions on the use of clean water interventions. Per Luquero et. al. (2013), the only long-term solution for cholera control is safe water and proper sanitation. Vanderslice and Briscoe (1993) argue that contaminated food supplies or improper hygiene are more important contributors to disease transmission rather than a clean water supply. According to Eisenberg, Scott, and Porco (2007), the effectiveness of water quality interventions is dependent on the level of sanitation that is found within the community.

Hand Washing and Hygiene Interventions

Sanitation, through hand washing and proper hygiene is important to cholera control. Improper hygiene practices can lead to further transmission of cholera, including through exposures related to sexual activity or through day-care centers. Without proper hygiene practices, contaminated water can increase transmission through activities such as bathing and washing activities (Eisenberg et al., 2007).

Waddington, Snilstveit, White, and Fewtrell (2009) conducted a review of cholera interventions and their effectiveness. Hygiene interventions, such as providing soap for hand-washing, were found to be effective in reducing the morbidity and mortality of cholera cases. In addition, there was no evidence of compliance with the hygiene intervention decreasing over time, which is observed with other interventions (Waddington et al., 2009).

Taylor et al. (2015) reviewed multiple cross-sectional studies that examined hygiene promotion during a cholera outbreak. One study suggested that the public health messages, regarding hygiene, were effective and promoted appropriate behavior changes. Another study reported large percentages of people receiving the health message with a majority employing at least one prevention method; however, the absence of baseline data made it impossible to conclude any behavior changes (Taylor et al., 2015).

Vaccine Interventions

There are two oral cholera vaccines prequalified by the WHO, Dukoral and Shanchol. Both vaccines are killed whole cell *V. cholera* O1 vaccines. In addition, Shanchol contains *V. cholera* O139 whereas Dukoral contains the recombinant cholera toxin B subunit. Both vaccines have a good safety and efficacy profile. The vaccines have an estimated 60-85% protection rate for a time span of 2-3 years. The WHO has recommended vaccine use since 2010; however, public health use has been limited due to questions about feasibility, acceptability, costs, and resources (Luquero et al., 2013).

Desai et al. (2015), conducted a double-blind, randomized, placebo-controlled trial within Ethiopia to examine the effectiveness of the killed whole-cell oral cholera vaccine. Both doses of the vaccine were administered to 106 adults and 106 children. There were no differences in rates of adverse events between the placebo and vaccine groups, no serious adverse events were noted, and no adverse events were noted within three days of dosing. The cholera vaccine elicited the anticipated immunological response in 81% of adults and 77% of children, supporting the effectiveness of the killed whole-cell oral cholera vaccine (Desai et al., 2015).

Between 2012 and 2014, a case-control study, within Haiti, was conducted to determine the field effectiveness of the oral inactivated bivalent whole-cell vaccine. This vaccine was found to be effective in protecting against cholera infections for up to 24 months after vaccination (Ivers et al., 2015). This study showed that the cholera vaccine campaign in Haiti was as effective as when a vaccine campaign was administered in historically cholera-endemic regions. Ivers et al. (2015) determined that vaccination campaigns are an important aspect of cholera control methods.

There are several limitations to a vaccination campaign. Both vaccines require a two-dose strategy, which can be difficult to coordinate. The vaccine must remain cold in temperature prior to administration, which can be logistically difficult. A vaccination campaign relies on the public's willingness to take the vaccination, therefore public awareness and education is necessary. Vaccination campaigns can also be labor intensive to conduct. In addition, availability of sufficient stockpiles of vaccines are lacking (Luquero et al., 2013).

In 2012, the Ministry of Health of Guinea organized the first cholera vaccine campaign in response to a cholera outbreak in Africa. This was also the first time that Shanchol was used in this manner within the African continent. Case management, hygiene, sanitation, water, and education interventions had already been implemented in response to the outbreak but were proving to be not effective at reducing transmission. This vaccination campaign provided high coverage and good acceptability within the rural population in guinea. Although the campaign was deemed successful, more research is needed to determine the feasibility of a campaign within densely populated urban scenarios where the cholera burden is high and outbreaks tend to evolve faster (Luquero et al., 2013).

Education Interventions

A key tool used in disease control is education and educational interventions. Educational interventions require investment in people and communities rather than a more biological approach. Educational interventions have the potential for high benefits with minimal costs. On the contrary, a lack of education can worsen the situation and increase the transmission of cholera. Cholera-specific educational interventions instruct symptomatic persons to seek medical attention promptly and of the importance of improving hygiene and sanitation practices (Edward & Nyerere, 2015).

There are several health education intervention barriers. In order for the intervention to be effective, the information must reach the intended audience, be correctly understood, gain attention, be accepted by the audience, and result in both a changed behavior and an improvement in health. In 1994, educational interventions were implemented during the cholera epidemic within Guinea-Bissau. These educational interventions, combined with local preventative rituals, word-of-mouth communication, and radio communications were found to be effective in reducing cholera transmission (Edward & Nyerere, 2015).

In 2005, Iran was faced with a cholera epidemic that incurred over 1,100 registered cholera cases. The epidemic stemmed from a locality in close proximity to a vegetable farm. Within this farm, workers were experiencing diarrhea episodes. Later testing confirmed cholera infections. This outbreak was originally suspected to be cholera-related and was quickly reported to health authorities. The initial response to the outbreak was local community education programs, education programs for local health professionals, and a strict control on food markets. In addition, a national propaganda campaign was launched to educate citizens on the hazards of fresh vegetables via all major communication routes. Public awareness and education, along with early detection and monitoring, were credited to the control of this epidemic that was stopped within four months (Lankarani & Alavian, 2013).

Tafuri, Guerra, Gallone, Cappelli, Lanotte, Quarto, and Germinario (2014), conducted a retrospective cohort study to examine the effectiveness of pre-travel counselling on the occurrence of travel-related diseases. It is estimated that between 20-64% of international travelers develop a health problem while abroad, many of which are gastrointestinal, dermatological or febrile diseases. Pre-travel counselling was shown to be effective in the prevention of diseases and in modifying the behavior of travelers (reducing high-risk conducts; Tafuri et al., 2014).

Mathematical Models

Several mathematical models have been developed to understand cholera dynamics. Liao and Wang (2011) developed a model examining three control methods; therapeutic treatment, vaccination, and water sanitation. This model did not incorporate educational interventions or a logistic growth of bacterium. In 2015, Edward and Nyerere expanded on Liao and Wang's model by adding an education control strategy along with the consideration that cholera bacteria grow logistically. This model determined that any single cholera control strategy (of the four that were examined) was more efficient at reducing cholera transmission over no control strategies. When two control strategies were combined, the most efficient combination was therapeutic treatment and education interventions. When three control strategies were combined, the most efficient combination was vaccination, therapeutic treatment, and education interventions. The model also showed that the most efficient control strategy was to adopt all four control methods concurrently (Edward & Nyerere, 2015). Edward and Nyerere (2015) concluded that the more control strategies that were implemented, the eradication of cholera was increased.

Camps of Internally Displaced Persons

Disasters (either man-made, biological, or weather-related) severely impact the health and economic status of a community. With natural disasters, the health of a community is effected immediately, with most deaths and injuries occurring within hours. Secondary effects are typically related to population displacement, public utility destruction, and the disruption of basic health services. Long-term health consequences ensue when food crops are destroyed or there is a prolonged population displacement, particularly in camps and settlements (Toole & Waldman, 1997).

Armed conflicts also have severe public health consequences. Since 1980, over 130 armed conflicts have occurred globally. Since 1980, it is estimated that over 1.5 million children have been killed in wars. In 1993, there were 47 active conflicts with 43 of them being internal wars. Armed conflicts severely impact civilian populations, resulting in increases mortality rates, forced migration, widespread human rights abuses, and the collapse of governance. There are several indirect health effects of armed conflicts due to population displacement, disruption of basic public health services, and food shortages. In recent years, there have been several examples of mass population movements. For example, the Kurdish exodus from northern Iraq in 1991, the Somalis migration in 1992, the Yugoslavia displacement in 1993 and 1995, and the migration of Rwandans in 1994 (Toole & Waldman, 1997).

Within these displaced populations, mass migration and food shortages are the number one cause of mortality following civil conflicts within Asia and Africa. The number of refugees (defined as those persons who flee their country due to fear of persecution) has steadily increased from 5 million in 1980 to over 20 million in 1994. In addition, over 25 million people had left their homes for the same fears; however, remain internally displaced in their home countries. The largest numbers of internally displaced persons are found in the Middle East, sub-Saharan Africa, within the republics of the former Soviet Union and the former Yugoslavia (Toole & Waldman, 1997).

High rates of malnutrition, morbidity, and mortality are seen in populations within internally displaced camps (CDC, 1992). The major health problems of internally displaced persons and refugees are the same; however, the health of internally displaced persons is often worse due to the inability of international relief agencies to offer support due to dangerous and difficult situations (Toole & Waldman, 1997). Deaths rates can reach as high as 60 times the crude mortality rate of those in non-refugee populations (CDC, 1992). The main causes of these high rates are attributed to diarrhoeal diseases, such as cholera (Connolly et al., 2004). Internally displaced persons also suffer more injuries as they are usually physically closer to areas of conflict than refugees are; however, both populations are extremely vulnerable to landmines as they migrate. Refugees are at a higher mortality risk once they arrive at their asylum due to inadequate medical care and inadequate food supplies both prior and during their migration. Limited mortality data is available for internally displaced persons (due to failures of families to report deaths, inaccurate estimates, lack of standard reporting procedures, and poorly representative population surveys); however, the data that is available suggests that mortality rates are extremely high (Toole & Waldman, 1997).

Primary prevention strategies are critical to internally displaced persons; however, reliable and safe epidemiological strategies are almost impossible. Traditional monitoring and evaluation of diseases and disease prevention can be ineffective in these situations (Toole & Waldman, 1997). Most emergencies that involve internally displaced persons occur in countries where there are insufficient resources to provide prompt assistance (CDC, 1992). Adequate shelter, safe water, proper sanitation, and immunization are often difficult within countries ravished with war due to the lack of resources (Toole & Waldman, 1997).

Primary prevention typically focuses on stopping the violence prior to food shortages and the migration of populations. Secondary prevention strategies include early detection, contingency planning, and personnel training. Tertiary prevention begins with preventing excess morbidity and mortality. Most of the deaths in these populations are preventable with current technologies. Relief programs must focus resources in addressing issues within the populations and then implementing interventions in a timely manner (Toole & Waldman, 1997).

Camps of internally displaced persons are at a high risk for cholera infections due to the lack of clean water, lack of proper sanitation, overcrowding of camps, and inadequate infrastructure within those camps (Edward & Nyerere, 2015). Within these camps, the provision of basic necessities is extremely difficult. Prolonged exposure to war and conflicts causes severe stress to refugees and displaced persons. Upon arriving at their destination, most refugees and displaced persons (typically women and children) suffer from severe depression and anxiety along with a loss of dignity due to dependence on others for their survival. If their destination is within close proximity of conflict, concerns of security increase the symptoms of stress and anxiety (Toole & Waldman, 1997).

Summary

As cholera continues to plague communities, it is essential to understand the history of cholera and how control measures have been used throughout the years in order to develop plans and policies to reduce the impact that cholera has in present day settings. High risk populations are highly susceptible to increased morbidity and mortality from cholera, including persons within camps of internally displaced persons. Current control measures need to be examined to determine effectiveness.

Chapter 3: Research Method

Introduction

The objective of this research was to conduct a retrospective comparison of cholera control measures within camps of internally displaced persons in order to determine whether historical control measures remain effective. In this chapter, I describe the research design and the rationale for using that design. In addition, the methodology for this research is presented, including a description of the study population and the data collection plan.

Research Design and Rationale

Research Question

The following quantitative research question drove this research: Did the cholera incidence rate and/or mortality rate change after the implementation of specific control measures/ combinations of control measures (proper sanitation, vaccination, and education) for internally displaced persons who experienced a cholera outbreak between the years 1996 and 2017?

Research Design

The nature of this study was quantitative. Quantitative research allows for the analysis of a phenomenon using numerical data (Yilmaz, 2013). The design of this study was a retrospective comparison with the different cholera control measures selected for the different cohorts. This design approach allowed for the examination of pre-existing longitudinal data that had been collected from cholera outbreaks. Per the Belmont Report, a prospective study design would not have been ethical, due to it being unethical to withhold applications of accepted best prevention practices from those in need (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979).

The hypothesis for this study was that changes in incidence and/or mortality rates after the implementation of specific cholera control measures or combinations of control measures within populations of internally displaced persons who experienced a cholera outbreak between the years 1996 and 2017 were different among the control measures or combinations of control measures. The null hypothesis was that there was no difference among the incidence and/or mortality rate changes after the implementation of specific cholera control measures/combinations of control measures within populations of internally displaced persons who experienced a cholera outbreak between the years 1996 and 2017. The dependent variables were incidence rate and mortality rate. The independent variables were the specific cholera control measures/combinations of control measures.

Role of the Researcher

Quantitative research relies on the researcher and the subjects being researched remaining separate and independent of each other (Yilmaz, 2013). Because this research involved the use of historical data, I remained independent of the data and primary data collection process. My role as the researcher was to retrieve and analyze data from secondary sources.

Methodology

Study Population and Sampling Strategy

The study population included individuals within camps of internally displaced persons who experienced a cholera outbreak. The following criteria determined whether specific populations were included in the study: (a) a cholera outbreak must have been declared within the WHO's *Weekly Epidemiological Record*, (b) the outbreak must have occurred within a camp of internally displaced persons, (c) control measures must have been documented in the WHO's Disease Outbreak News, and (d) the outbreak must have occurred between 1995 and 2017 (WHO, 2016a, 2016b). These criteria were used to ensure that all characteristics and parameters within the outbreaks (such as sanitation conditions and clean water supplies) were consistent.

Contingency Plan

If there had not been enough data to analyze when looking at camps of internally displaced persons, the research would have been expanded to include additional populations within countries that were impacted by cholera outbreaks between the years 1996 and 2017.

Instrumentation

This research used categories based on the cholera control measures that were implemented, such as vaccination campaigns and education programs. The specific cohorts were determined from the data on each outbreak.

Data

WHO incidence and fatality data from outbreaks occurring between 1995 and 2017 were examined prior to and after implementation of control measures to determine how control measures impacted incidence and mortality rates. Per the International Health Regulations, cases of cholera require notification to the WHO, and these cases are published in the *Weekly Epidemiological Record* (WHO, 2016b). The *Weekly Epidemiological Record* provides listings that indicate the country that was impacted, the year that the outbreak occurred, the number of reported cases, the number of reported deaths, and implied fatality rates (WHO, 2016b). The World Bank (2018) provides country population data for calculations of incidence and mortality rates.

The WHO (2016a) uses Disease Outbreak News releases (DONs) to report on responses to outbreaks. DONs provide information on what control measures were implemented, the timing of responses and control measures, what the public health response was, and where outbreaks were occurring (including if they are occurring within camps of internally displaced persons). I used DONs in this study to examine what control measures were implemented, the timing of implementation, and the population in which the outbreak occurred. Because the DONs had data from 1996 to 2017, I focused on this time period for analysis.

Data Analysis Plan

The DONs were used to identify cholera outbreaks in camps of internally displaced persons between 1996 and 2017. Once the outbreak and the year of occurrence had been identified using the *Weekly Epidemiological Record*, DONs were used to examine case and mortality rates before and after the implementation of control measures.

The dependent variables were incidence rate and mortality rate. The independent variables were the specific cholera control measures/combinations of control measures (water quality intervention, sanitation intervention, hand washing and hygiene intervention, vaccine intervention education intervention, or a combination). Data were compiled and grouped into categories based on the control measure(s) that were implemented. Data were analyzed using SPSS.

Adjusted statistics were used to enable fair comparisons among the cohorts. Cohorts were determined based on the cholera control measures that were implemented in each of the camps. To ensure that the comparison was objective, studied outbreaks included those occurring within camps of internally displaced individuals only. Any other confounding variables (such as geographical location, population dynamics, or time period of outbreak) were adjusted through statistical analysis (using statistical methods such as stratification or ANCOVA) to reduce the impact that the confounding variables had on the analysis of the independent variables.

Issues of Trustworthiness

Validity, how well a research concept is measured, is broken down into content validity, construct validity, and criterion validity. Content validity is the extent to which an instrument measures all aspects of the variable it was set to measure (Heale & Twycross, 2017). The instrument in this research, the defined categories, had strong content validity due to being pulled directly from the dataset. Construct validity is the extent to which an instrument measures the variable that it was intended to measure. There are three forms of evidence to demonstrate construct validity: homogeneity, convergence, and theory evidence (Heale & Twycross, 2017). To ensure homogeneity and to reduce convergence, each defined category measured only one variable/ combination of variables, and each data point was placed into the most appropriate category. Criterion validity is the extent to which another instrument measures the same variable (Heale & Twycross, 2017). The categories were defined from the dataset. Each data point was placed into only one category, the one that most appropriately labeled the control measure(s) that were used.

Reliability refers to the consistency of measurements. The attributes of reliability include homogeneity (internal consistency), stability, and equivalence (Heale & Twycross, 2017). To ensure homogeneity (internal consistency), stability, and equivalence, a structured decision tool was developed and used to ensure that all data points were consistently put into categories.

Summary

This study employed a retrospective comparison with the different cholera control measures selected for the different cohorts (determined from the dataset). Data were compiled from the *Weekly Epidemiological Record* and DONs. Adjusted statistics were used for comparisons. Steps were taken to ensure high validity and reliability.

Chapter 4: Results

Introduction

The purpose of this quantitative study was to conduct a retrospective comparison of cholera control measures within camps of internally displaced persons to determine whether historical control measures remain effective in present-day settings. Data was collected from the WHO and the World Bank. ANCOVA methods were used to examine any statistical significance among the control measures in relation to changes in case or death rates due to the implementation of those control measures.

Data Collection

Data was retrieved from the WHO Data Repository via the WHO website. Per the International Health Regulations, cases of cholera require notification to the WHO, and these reports are published in the *Weekly Epidemiological Record* (WHO, 2016b). The *Weekly Epidemiological Record* provided a listing of the country in which an outbreak occurred, the number of reported cases, and the number of reported deaths associated with the outbreak (WHO, 2016b). Country population statistics were gathered from the World Bank via an online data repository to calculate incidence and mortality rates (The World Bank, 2018).

DONs, available via the WHO website, provided information on reported outbreaks, including what control measures were implemented, timing of responses and control measures, what the public health response was, and where the outbreak occurred (including if an outbreak was occurring within camps of internally displaced persons). Less than 1% of DONs (17 out of the 271 reviewed) contained all of the above-listed information for each outbreak record. Additional data and datasets were not used, in order to ensure that the available data was consistent and from a reliable source for analysis.

Data Analysis

Microsoft Word and Microsoft Excel were used to organize the data that was retrieved from the WHO. The DONs were reviewed to identify cholera outbreaks within camps of internally displaced persons. Between 1996 and 2018, 42 DON reports covering 18 different countries identified cholera outbreaks as occurring within camps of internally displaced persons. Each of these 42 reports was then reviewed to determine whether it matched the criteria listed in Chapter 3 to be included within the analysis sample. The criteria were as follows: (a) a cholera outbreak must have been declared within the WHO's *Weekly Epidemiological Record*, (b) the outbreak must have occurred within a camp of internally displaced persons, (c) control measures must have been documented in the WHO's Disease Outbreak News, and (d) the outbreak must have occurred between 1995 and 2017 (WHO, 2016a, 2016b). Criterion (c) states that control measures must have been documented in the DONs in order for the outbreak to be included; however, four reports without documented primary control measures within the DONs were included in the data set to increase statistical power and provide an additional cohort for comparison. It can be assumed that control measures were implemented during these outbreaks, even though they were not documented within the reports used for this analysis. Reports were then sorted by country and put into chronological order. Control measures for each report were recorded and placed into the following categories:

- A—Establishment of weekly meetings, increased surveillance, and public health responder training
- V—Vaccinations
- C—Mass chlorination of water supplies
- N—No actions recorded
- R—Response team activated
- E—Educational campaign
- S—Increased surveillance initiated
- W—Increased medical supplies, clean water, and water, sanitation, and hygiene (WASH) practices

The WHO Data Repository was used to gather frequencies of reported cholera cases and cholera deaths per year. Case, death frequencies, and overall population totals (from the World Bank) were used to calculate incidence and mortality rates for the previous year and the year of the report. For example, if a DON outbreak report had a date of February 10, 1998, the data from 1997 and 1998 were used for comparison. Changes in incidence and mortality percentages between the years in which control measures were implemented were then calculated using the following equation:

([ending year rate – beginning year rate] / beginning year rate) * 100

The percentage change was calculated to minimize confounding based on the population size, the outbreak size, and the size of the country in which the outbreak occurred. If either year (beginning or ending) was not present within the WHO Data Repository, the outbreak was excluded from the dataset. In addition, if the DON reported cases or deaths that were not consistent with the yearly totals from the WHO Data Repository, that data point was eliminated due to validity concerns (e.g., if a DON reported more frequencies of cases and/or deaths than the WHO Data Repository reported for that year, the data point was excluded). In total, there were 16 outbreaks within the analysis dataset for cholera case analysis and 12 outbreaks within the analysis dataset for cholera death analysis. See Table 1 for incidence rate information and Table 2 for mortality rate information.

Table 1

Incidence Rates and Percent Changes

Year			Incidence rate			Control measure	
Start	End	Country	Start year	End year	Percent change	Primary	Secondary
1995	1996	Burundi	38.53	6.92	-82.04	W	N
1995	1996	Liberia	164.94	407.18	146.87	N	N
1995	1996	Rwanda	0.05	1.73	3360.00	N	N
1995	1996	Tanzania	9.87	4.75	-51.87	W	S
1996	1997	Burundi	6.92	32.05	363.15	S	N
1997	1998	Afghanistan	22.69	53.01	133.63	R	W
1997	1998	DRC[a]	29.66	420.65	1318.24	W	N
1997	1998	Rwanda	4.20	45.61	985.95	N	N
2002	2003	Liberia	36.40	1114.81	2962.66	C	W
2009	2010	Nigeria	8.87	28.03	216.01	N	N
2011	2012	DRC[a]	216.41	331.47	53.17	E	S
2012	2013	Mexico	0.00	0.15	15.00	A	N
2014	2015	DRC[a]	213.37	182.19	-14.61	S	W
2014	2015	Iraq	0.00	13.75	1375.00	A	V
2016	2017	Kenya	12.10	0.00	-100.00	R	N
2016	2017	Mozambique	3.06	0.00	-100.00	A	N

Note. All incidence rates were calculated per 100,000 persons.
[a]Democratic Republic of Congo.

Table 2

Mortality Rates and Percent Changes

Year			Mortality rate			Control measure	
Start	End	Country	Start year	End year	Percent change	Primary	Secondary
1995	1996	Liberia	0.69	0.92	33.33	N	N
1995	1996	Rwanda	0.00	0.05	5.00	N	N
1995	1996	Tanzania	0.52	0.20	-61.54	W	S
1996	1997	Burundi	0	0.52	52.00	S	N
1997	1998	Afghanistan	0.68	0.00	-100.00	R	W
1997	1998	DRC[a]	1.77	15.92	799.44	W	N
1997	1998	Rwanda	0.09	0.40	344.44	N	N
2002	2003	Liberia	0.00	0.21	21.00	C	W
2009	2010	Nigeria	2.34	9.31	297.86	N	N
2011	2012	DRC[a]	3.18	4.46	40.25	E	S
2012	2013	Mexico	0.00	0.01	1.00	A	N
2014	2015	DRC[a]	2.02	1.50	-25.74	S	W

Note. All mortality rates were calculated per 100,000 persons.
[a]Democratic Republic of Congo.

Data was then imported into SPSS (version 23) for ANCOVA analysis. For the cholera incidence rate ANCOVA analysis, the dependent variable was the incidence rate percent change between the years, the independent variable was the first and second control measure implemented, and the covariates were the start year and ending year. For the cholera mortality rate ANCOVA analysis, the dependent variable was the mortality rate percent change between the years, the independent variable was the first and second control measure implemented, and the covariates were the start year and ending year. Factor interactions were analyzed for Control Measure 1, Control Measure 2, and then the combination of Control Measure 1 and 2. The confidence interval adjustment was completed with the Bonferroni method. In addition, descriptive statistics, estimates of effect size, and homogeneity tests were completed. A 95% confidence interval was used. ANCOVA results are shown in Tables 3 and 4.

Table 3

Cholera Case ANCOVA Results

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Corrected Model	79600528.837[a]	11	7236411.712	3.171	.186	.921
Intercept	.000	0	.	.	.	.000
StartYear	.000	0	.	.	.	.000
EndYear	.000	0	.	.	.	.000
Action1	56852556.680	5	11370511.336	4.982	.108	.893
Action2	44121444.886	3	14707148.295	6.444	.080	.866
Action1 * Action2	573321.147	1	573321.147	.251	.651	.077
Error	6847191.152	3	2282397.051			
Total	109661630.797	15				
Corrected Total	86447719.989	14				

a. R Squared = .921 (Adjusted R Squared = .630)

Table 4

Cholera Death ANCOVA Results

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Corrected Model	35147835.246[a]	9	3905315.027	.128	.989	.365
Intercept	.000	0	.	.	.	.000
StartYear	.000	0	.	.	.	.000
EndYear	.000	0	.	.	.	.000
Action1	11416916.668	4	2854229.167	.093	.975	.157
Action2	1009739.618	2	504869.809	.017	.984	.016
Action1 * Action2	.000	0	.	.	.	.000
Error	61075267.186	2	30537633.593			
Total	115333189.867	12				
Corrected Total	96223102.432	11				

a. R Squared = .365 (Adjusted R Squared = -2.491)

Cohorts

Reports were assigned into one of the following cohorts based on the information documented within the DONs. A structured decision method was used to assign cohorts. After identification of an outbreak and confirmation that the outbreak conformed to the study criteria (as outlined previously), control measures were identified within the DONs. Typically, control measures were specifically listed out and described within the DON report. Once the control measure had been identified within the report, it was documented. Once all reports had been reviewed, the control measures were grouped together based on the similar information/measures. Documentation of control measures within the DONs was consistent, and the control measure grouping was evident.

If multiple cholera control measures were reported, the first/major control measure was identified, and then it was assigned to the report as the main control measure. Any additional cholera control measures were assigned as the secondary control measure. Not all reports had multiple or secondary control measures reported; therefore, the secondary control measure was documented as Cohort N.

Cohort A

Cohort A was defined for when the following control measures were implemented: the establishment of weekly meetings to assess the cholera situation in that country, increased cholera surveillance, and training for public health responders. There were three reports included in the analysis dataset that had these control measures listed as the primary method and zero reports that had these control measures listed as the secondary method.

Cohort V

Cohort V was defined for the implementation of a mass vaccination campaign of either Dukoral and Shanchol. There were zero reports in the analysis dataset that had this control measure listed as the primary method; however, there was one report that had this control measure listed as the secondary method. The specific vaccine that was used in the vaccination campaign was not identified within the DON; however, additional resources identified that the vaccine campaign used Shanchol (Lam et al., 2017).

Cohort C

Cohort C was defined for the mass chlorination of water supplies. There was one report that had this control measure listed as the primary method and zero reports that had this control measure listed as the secondary method.

Cohort N

Cohort N was defined for when no control methods/actions were documented within the DONs. There were four reports that had no control measures listed as the primary method and 11 reports that did not have any secondary method listed.

Cohort R

Cohort R was defined as the activation of a response team for the cholera outbreak. There were two reports that had this control measure listed as the primary method and no reports that had this control measure listed as the secondary method.

Cohort E

Cohort E was defined as an educational campaign. There was one report that had this control measure listed as the primary method and zero reports that had this control measure listed as the secondary method.

Cohort S

Cohort S was defined for when increased surveillance was initiated as the primary response. This cohort differed from Cohort A due to Cohort S being used when only increased surveillance was listed as the control measure. There were two reports that had this control measure listed as the primary method and two reports that had this control measure listed as the secondary method.

Cohort W

Cohort W was defined by an increased amount of medical supplies, increased clean water availability/supplies, and increased sanitation and hygiene practices (WASH). Historically, education campaigns accompany these control measures; however, they were not included with the control measure listing in the DONs. There were three reports that had this control measure listed as the primary method and three reports that had this control measure listed as the secondary method.

Evidence of Trustworthiness

Validity

Content validity is the extent to which an instrument measures all aspects of the variable it was set to measure (Heale & Twycross, 2017). The instrument in this research, the defined categories, had strong content validity due to the cohorts being pulled directly from the dataset.

In addition, the validity of the DONs was evaluated. Due to regulations, cholera infections must be reported to the WHO, the producer of the DONs. Collier (2010) examined online reporting of diseases and determined that raw news counts typically had results that reflected how the reader population felt about the outbreak versus the actual population at risk. As the DONs were used to examine case and death reports, it was determined to be a reliable source for the information contained within the report. It is important to note that any source of cholera case or mortality reports does not adequately reflect the global cholera burden because of underreporting (Ali et al., 2012).

Construct validity is the extent to which an instrument measures the variable that it was intended to measure. There are three forms of evidence to demonstrate construct validity: homogeneity, convergence, and theory evidence (Heale & Twycross, 2017). To ensure homogeneity and to reduce convergence, each defined category measured only one variable or specific combination of variables, and each data point was placed into the most appropriate category only. Data points were placed into only one cohort.

Criterion validity involves the extent to which another instrument measures the same variable (Heale & Twycross, 2017). The cohorts were defined directly from the dataset. Each outbreak was placed into only one cohort that was identified from the DONs. Another instrument would be able to place the outbreaks into the same cohorts, as the cohorts were identified from the information provided within the DONs.

Reliability

Reliability refers to consistency of measurements. The attributes of reliability include homogeneity (internal consistency), stability, and equivalence (Heale & Twycross, 2017). To ensure homogeneity (internal consistency), stability, and equivalence, a structured decision method (described previously) was used to ensure that all data points were consistently put into the appropriate categories. This consisted of identifying the first control measure (and secondary measure, when applicable) and placing the outbreak into the appropriate cohort based on the information described within the DONs. Cholera control measures have been fairly consistent over the years, with consistent documentation of control measures within the DONs; therefore, identification of the proper cohort was not a challenge within this research and was consistent.

Results

This study's quantitative research question was addressed through data that was retrieved from the WHO on reported cholera outbreaks and control measures used during those outbreaks. The research question was the following: Did the cholera incidence rate and/or mortality rate change after the implementation of specific control measures/combinations of control measures (proper sanitation, vaccination, and education) within groups of internally displaced persons that experienced a cholera outbreak between the years of 1996 and 2017? Cholera outbreaks within camps of internally displaced persons were identified from the DONs. The control measures that were implemented within those outbreaks were then placed into cohorts. The WHO Data

Repository was used for case and death rates for the year prior to the outbreak and the ending year of the outbreak. The case percent change and death percent change were calculated for each outbreak report that contained data from both years. ANCOVA methods were used to examine any statistical significance in the case or death percent change depending on the control measure that was implemented. ANCOVA methods were used to examine significance in the primary control measure, the secondary control measure, and the combination of the primary and secondary control measures. Through the ANCOVA tests, there were no statistically significant changes in cases (incidence rate) or deaths (mortality rate) based on the primary control measure, the secondary control measure, or the combination of the primary and secondary control measures.

Summary

In summary, cholera outbreaks within camps of internally displaced persons were identified from the DONs between the years 1996 and 2017. The control measures that were implemented within those outbreaks were then placed into standardized cohorts. The WHO Data Repository was used for case and death rates for the year prior to the outbreak and the year of the outbreak for the country that the DONs reported an outbreak in; then the case percent change and death percent change were calculated for each outbreak report. ANCOVA methods were used to examine any statistical significance in the case or death percent change depending on the control measure that was implemented. No statistically significant changes were observed through these methods.

Chapter 5: Discussion, Conclusions, and Recommendations

Introduction

The purpose of this quantitative study was to conduct a retrospective comparison of cholera control measures within camps of internally displaced persons to determine if historical control measures remain effective in present-day settings. A quantitative approach was used to ascertain whether there were changes in cholera incidence rate or cholera mortality rate dependent on the implementation of primary, secondary, or a combination of both primary and secondary control measures. ANCOVA methods were used to examine any statistical significance among the control measures. No statistical significance was noted in the change of incidence or mortality rates based on the implementation of primary, secondary, or a combination of both primary and secondary control measures.

Interpretation of Findings

There were no statistically significant findings within this study. The current dataset indicates that there was not a difference in incidence or mortality rates based on the control measure or combinations of control measures that were implemented. The current data show that implementation of any control measure, including taking no action (Cohort N), is equivalent in terms of reducing cholera cases and/or deaths during a cholera outbreak within a camp of internally displaced persons. These results go against the published literature and the recommendations of the WHO on cholera control.

Per the WHO, a multifaceted approach (including a combination of surveillance, WASH, medical treatments, and vaccine use) is crucial to reducing cholera cases and deaths (WHO, 2018). This multifaceted approach is essential for populations of internally displaced persons, in which the cholera at-risk rate remains highest. The results from this research are not logical based on the literature and WHO recommendations, primarily due to the limitations listed below.

As a group, camps of internally displaced persons face numerous challenges. Displacement of populations severely impacts the health and economic status of a community, with most deaths and injuries occurring within hours. Additional effects are typically related to population displacement, public utility destruction, and the disruption of basic health services. Long-term health consequences ensue when food crops are destroyed or with prolonged population displacement, particularly in camps and settlements (Toole & Waldman, 1997). The major health problems of internally displaced persons are often worsened due to the inability of international relief agencies to offer support because of the dangerous and difficult situations surrounding camps or routes to the camps (Toole & Waldman, 1997). This situation leads to increased death rates, which may be as high as 60 times the crude mortality rate of those in nonrefugee populations (CDC, 1992). These challenges impact the ability of control measures to not only be implemented, but also be effective, thus resulting in continued increases in cholera cases and deaths.

Within Tables 1 and 2, several positive percentage changes were noted in both incidence and mortality rates after the implementation of control measures. There were 11 out of 16 incidence rate changes that were positive and nine out of 12 mortality rate changes that were positive. There are several possible explanations for this phenomenon.

Going against logical explanation, these positive changes may indicate that the implementation of cholera control measures did not aid in reducing incidence and mortality rates, but rather allowed rates to continue to increase. Another explanation is that data were not collected for the entire length of the outbreak. As outbreaks typically follow a bell curve, the available data might only represent the beginning or part of that curve. As previously mentioned, camps of internally displaced persons face several challenges that can lead to difficulties in implementation and effectiveness of control measures during an outbreak.

An overall trend did appear during data organization. Beginning with the reports from 2013, within camps of internally displaced persons, the control measures became consistent with those outlined in Cohort A, with eight of the 12 reports (between 2013 and 2017) falling into Cohort A control measures. In 2008, the WHO published an outbreak communication planning guide that outlined several steps to implement during an outbreak. It recommended the following steps to take during an outbreak: assessment, proper planning for communication and coordination, communication strategy, assigning responsibilities and stakeholders, and monitoring (WHO, 2008). These are all attributes of the control measures listed in Cohort A, and the publication of this guide could explain why the control measures became standardized after it became available.

In addition, within the text of the DONs, vaccine campaigns were discussed in several initial reports but were not implemented until later updates, if at all. This could be attributed to the costs associated with vaccine campaigns, along with the logistics needed to implement a campaign. There are other more economical control measures that can be implemented while the logistics of a vaccine campaign are coordinated, which could explain the later timing of vaccine campaigns.

A Wilcoxon signed-rank test was used to examine similarities between the incidence and mortality rate changes after the implementation of cholera control measures. For comparison of incidence rate changes, due to implementation of primary control measures, the most favorable in reducing cholera incidence rates were Cohort R, Cohort A, and Cohort W. Those that were the least favorable to an incidence rate reduction were Cohort N and Cohort C. For secondary control measures, Cohort W and Cohort S were the most favorable in reducing cholera incidence rates, whereas Cohort N was the least favorable for reducing incidence rates. With regards to mortality rate changes, the control measures that were the most favorable in reducing mortality raters were Cohort R, Cohort W, and Cohort S. The least favorable was Cohort N. Consistent with the incidence rate changes, for secondary control measures, Cohort W and Cohort S were the most favorable, whereas Cohort N was the least favorable in reducing mortality rates. These results are in line with historical cholera outbreak management with Cohort N (taking no action) being ranked, in both primary and secondary control measures, at being the least likely to reduce incidence/mortality rates. Cohort W, Cohort R, and Cohort S were all favorable in reducing incidence and mortality rates, either as a primary or secondary control measure. These three cohorts all contain cholera control measures that align with the WHO recommendations during a cholera outbreak.

Limitations of the Study

As with any research, there were several limitations to this study. The first limitation to this research was the analyzed sample size. While 42 reports were noted as pertaining to outbreaks occurring within camps of internally displaced persons, only 16 of those reports were able to be included within the primary control measure dataset due to the availability of all of the appropriate data points for analysis. More outbreaks may have occurred within camps of internally displaced persons; however, the DON was missing that documentation and therefore that outbreak was not included within the analysis. With the magnitude of DONs, it was not possible to research each unspecified report to determine whether it occurred within a camp of internally displaced persons. In addition, the four reports occurring in 2018 were not included due to year-end data availability issues. Increased samples would increase the statistical power of the study and provide for a more robust comparison among the control measures.

Cholera outbreaks are required to be reported to the WHO; however, only approximately 5%-10% of cholera cases are actually reported within underdeveloped settings. Thus, underreporting was also a limitation of this study (Ali et al, 2012). There were several surveillance and reporting limitations, including economic disincentives, such as trade sanctions and tourism limitations that can be detrimental to a country's economy, which may lead a country to underestimate and underreport its true cholera burden (Zuckerman et al., 2007). Due to potential underreporting by individual countries, the WHO Data Repository was used within this analysis to ensure consistency among the data. Additional data sources were not included in the data set due to concerns of data consistency and availability of reliable sources.

Another limitation was that the yearly totals for the year prior and year end were used. These data allowed for the analysis but could potentially confound the results due to the timing of the implementation of the control measure compared to either of the yearly totals. For example, the percent change of either cases or deaths could be skewed if the DON report was from January rather than December. Because not all outbreaks had multiple DON reports to use for case/death percent change information, data from the WHO Data Repository were needed for the analysis.

In addition, yearly totals were for the entire country and were not limited to the camp in which the documented outbreak occurred. This could compound the data if additional cholera cases or deaths were reported outside the camp of internally displaced people. Additional research could limit the yearly totals to only include outbreak data from within the camps of internally displaced persons.

Another limitation was that not all reports had control measures listed. These were included in the analysis for greater statistical power; however, it can be assumed that some of these reports did in fact have control measures implemented that were just not documented. Without these values, the ANCOVA cannot be run due to the limited number of samples.

Recommendations

Further research should be conducted to determine why the incidence rate and mortality rate for cholera remain high, especially within camps of internally displaced persons, who represent populations at high risk of the disease. Using the current research design, the use of additional resources to identify (a) outbreaks within camps of internally displaced persons, (b) specific control measures that were implemented, and (c) accurate case and death rates would increase the ability of statistical methods to determine if there are any differences between the control measures. The current research did not find any statistical significance; however, an increased sample size might change that result.

Additional research should be conducted to determine whether control measures are adequate among outbreaks within populations of internally displaced persons when compared to outbreaks within the general population. The question of whether the control measures provide the same response within these two populations should be explored. This research could provide additional information on which control measure is the most appropriate to use in a specific population to reduce incidence and death rates.

In addition, given that a trend was noted in the control measures that were being implemented, further research into the structured response plan is needed to ensure that it is working appropriately and to determine if any modifications are needed. Further, research on the implementation of vaccine campaigns could reduce the time needed for implementation and thus reduce the cholera burden.

Implications and Social Change

This study raises the question of why there are so many cholera cases and deaths each year when there are several control measures available. The results of this research show that there is no benefit or added risk with the implementation of any cholera control measure—a finding that goes against the literature and WHO recommendations. Cholera is a major public health burden, especially in camps of internally displaced persons where the population is at greater risk. Although this research did not produce significant results or expected results, it can be used as a basis for continued research.

The Global Task Force on Cholera (GTFCC) is committed to reducing cholera infections by 90% by the year 2030. The GTFCC has declared that cholera control is not only a moral obligation, but also a step toward reducing health inequality in the world's most vulnerable populations. The GTFCC is committed to supporting countries that are facing a cholera outbreak by assisting with earlier outbreak detection, responding to the outbreak immediately, and containing the outbreak as rapidly as possible (GTFCC, 2017). This research supports efforts made by the GTFCC and its Global Roadmap by examining cholera control measures and attempting to identify the most effective control measure to reduce the burden of cholera for these vulnerable populations.

Conclusions

The purpose of this quantitative study was to conduct a retrospective comparison of cholera control measures within camps of internally displaced persons in order to determine whether historical control measures remain effective in present-day settings. A quantitative approach was used to determine whether there were changes in incidence rate or mortality rate dependent on the implementation of primary, secondary, or both primary and secondary control measures. ANCOVA methods were used to examine any statistical significance among the control measures. No statistical significance was noted due to the implementation of primary, secondary, or both primary and secondary control measures. Limitations of this study provide the basis for continued research on this topic.

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Appendix A: DON Websites

Country	Date	URL to DON
Afghanistan	21Aug1998	http://www.who.int/csr/don/1998_08_21/en/
	02Sep1998	http://www.who.int/csr/don/1998_09_02/en/
Burundi	22Jan1996	http://www.who.int/csr/don/1996_01_22f/en/
	09Jan1997	http://www.who.int/csr/don/1997_01_09a/en/
	17Jan1997	http://www.who.int/csr/don/1997_01_17b/en/
Democratic Republic of Congo	06Jan1998	http://www.who.int/csr/don/1998_01_06a/en/
	19May1998	http://www.who.int/csr/don/1998_05_19b/en/
	23Jul2012	http://www.who.int/csr/don/2012_07_23/en/
	15Dec2015	http://www.who.int/csr/don/15-december-2015-cholera-drc/en/
Iraq	28Sep2015	http://www.who.int/csr/don/28-september-2015-cholera/en/
	26Nov2015	http://www.who.int/csr/don/26-november-2015-iraq-cholera/en/
	12Oct2015	http://www.who.int/csr/don/12-october-2015-cholera/en/
Kenya	21Jul2017	http://www.who.int/csr/don/21-july-2017-cholera-kenya/en/
	11Dec2017	http://www.who.int/csr/don/11-december-2017-cholera-kenya/en/
Liberia	26Apr1996	http://www.who.int/csr/don/1996_04_26/en/
	03Jul2003	http://www.who.int/csr/don/2003_07_03a/en/
	15Jul2003	http://www.who.int/csr/don/2003_07_15/en/
	13Aug2003	http://www.who.int/csr/don/2003_08_13/en/
	02Sep2003	http://www.who.int/csr/don/2003_09_02/en/
	30Sep2003	http://www.who.int/csr/don/2003_09_30/en/
Mexico	19Oct2013	http://www.who.int/csr/don/2013_10_19_cholera/en/
	28Oct2013	http://www.who.int/csr/don/2013_10_28/en/
	13Nov2013	http://www.who.int/csr/don/2013_11_13/en/
	25Nov2013	http://www.who.int/csr/don/2013_11_25/en/
Mozambique	April 2017	http://www.who.int/csr/don/19-february-2018-cholera-mozambique/en/
Nigeria	08Oct2010	http://www.who.int/csr/don/2010_10_08/en/
Rwanda	13Dec1996	http://www.who.int/csr/don/1996_12_13a/en/
	22Oct1998	http://www.who.int/csr/don/1998_10_22c/en/
Tanzania	04Dec1996	http://www.who.int/csr/don/1996_12_06c/en/